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Examining Group 1652 1/83

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

In re Application of: Coleman et al.

Title: A NOVEL HUMAN JAK2 KINASE

Serial No.: 09/467,100

Filing Date:

December 10, 1999

Examiner: Hutson, R.

Group Art Unit:

1652

Box AF

Commissioner for Patents

Washington, D.C. 20231

REPLY BRIEF

Sir:

I. Introduction

This is Appellants' Reply Brief On Appeal (submitted in triplicate) in response to the Examiner's Answer dated July 30, 2002 ("the Examiner's Answer") in the above-identified application (the Coleman '100 application).

In the Examiner's Answer the Patent Examiner:

(1) maintained the rejection of Claims 36-40 under 35 U.S.C. § 112, first paragraph for alleged lack of enablement, because of an alleged inadequate disclosure of how to use the claimed polynucleotide variants;

(2) maintained the rejection of Claims 36-40 under 35 U.S.C. § 112, first paragraph for alleged lack of written description of the claimed polynucleotide variants;

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(3) maintained the rejection of Claims 36-40 under 35 U.S.C. § 112, first paragraph for alleged lack of written description of the claimed polynucleotide variants, with respect to alleged “new matter”;

(4) maintained the rejection of Claims 37-40 under 35 U.S.C. § 103(a) for alleged obviousness of the claimed methods over Silvennoinen et al.;

(5) maintained the rejection of Claims 30-36 under 35 U.S.C. § 101 under the judicially created doctrine of obviousness-type double-patenting over Claims 1-3 of U.S. Patent No. 5,914,393; and

(6) maintained the rejection of Claims 37-40 under 35 U.S.C. § 101 under the judicially created doctrine of obviousness-type double-patenting over Claim 10 of U.S. Patent No. 5,914,393.

II. Comment on the Appeal Brief’s “Summary of Invention”

Appellants acknowledge the Examiner’s objection to the “Summary of Invention” in Appellants’ Appeal Brief. (Examiner’s Answer, page 2.) However, Appellants do not agree.

III. Submission of the Bedilion Declaration, the toxicology testing references, and the Brenner reference were for “good and sufficient reasons”

A. Bedilion Declaration

On page 13, the Examiner asserts that the Declaration of Dr. Tod Bedilion (submitted with the Appeal Brief on May 9, 2002) “for the purpose of this answer have not been considered.” The Advisory Action mailed July 30, 2002 further states that “[t]he affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.” Appellants do not understand this reason for refusing to consider the Declaration. See 37 CFR 1.195: “Affidavits, declarations, or exhibits submitted after the case has been appealed will not be admitted without a showing of good and sufficient reasons why they were not earlier presented.”

Appellants submitted arguments for the use of the claimed polynucleotide variants in toxicology testing in the Response to Non-Final Office Action filed June 13, 2001, but Examiner did not address

or even mention Appellants' arguments in the Final Office Action. The Examiner in the Final Office Action mailed August 28, 2001 merely repeated the rejection from the March 13, 2001 Office Action. Therefore, Appellants were compelled to re-submit these arguments in the Appeal Brief, further supported by the Bedilion Declaration. This is the statutorily required "good and sufficient" reason why it was not earlier presented.

B. Toxicology Testing References

The Examiner states that "Appellants provide a number of citations in support of their argument of the prevalence, advantages, and importance of gene expression profiling in toxicology testing, drug development, and disease diagnosis, however for the purpose of this brief, these references have not been considered because these appellants have not shown good and sufficient reasons why they were not presented earlier." (Examiner's Answer, page 16.) Appellants note that the following references cited in the Appeal Brief filed May 9, 2002 were "presented earlier" in the Response to Non-Final Office Action filed June 13, 2001 and therefore should be considered by the Examiner. Appellants note that the Examiner did not address these references in the Final Office Action and therefore Appellants were compelled to re-cite them in the Appeal Brief.

John C. Rockett, et. al., Differential gene expression in drug metabolism and toxicology: practicalities, problems, and potential, Xenobiotica 29:655-691 (July 1999) (Reference No. 1 in the Appeal Brief; Reference No. 2 in Response filed June 13, 2001);

Emile F. Nuwaysir, et al., Microarrays and Toxicology: The Advent of Toxicogenomics, Molecular Carcinogenesis 24:153-159 (1999) (Reference No. 2 in the Appeal Brief; Reference No. 3 in Response filed June 13, 2001);

Sandra Steiner and N. Leigh Anderson, Expression profiling in toxicology -- potentials and limitations, Toxicology Letters 112-13:467-471 (2000) (Reference No. 3 in the Appeal Brief; Reference No. 1 in the Response filed June 13, 2001);

John C. Rockett and David J. Dix, Application of DNA Arrays to Toxicology, Environ. Health Perspec. 107:681-685 (1999) (Reference No. 4, see page 683 in the Appeal Brief; Reference No. 4 in Response filed June 13, 2001); and

Email from the primary investigator on the Nuwaysir paper, Dr. Cynthia Afshari, to an Incyte employee, dated July 3, 2000, as well as the original message to which she was

responding (Reference No. 5 in the Appeal Brief; Reference No. 5 in Response filed June 13, 2001).

C. Brenner Reference

The Examiner has not considered the Brenner reference because it was submitted after Final Rejection (Examiner's Answer, pages 18-19.) Appellants submit that the Brenner reference is a fundamental teaching in the art, the teachings of which Appellants expect an Examiner and anyone with sufficient skill in the art to be familiar. Therefore, the Brenner reference is presented to make the point regarding the sufficiency of homology that the Examiner is attempting to ignore.

IV. **Enablement rejection**

A. Biological function is irrelevant to utility

The Examiner states that "[a] naturally occurring amino acid¹ sequence having at least 92% sequence identity to the polynucleotide sequence of SEQ ID NO:1" encompasses polynucleotide variants encoding naturally occurring orthologs in related species, particularly human polynucleotide variants with mutations that result in altered activity. It is unclear what function a polypeptide variant with a mutation that results in 'altered activity' has and absent a teaching of this 'specific altered activity', how the polynucleotides which encode these polypeptides are enabled with respect to there [sic: their] use." (Examiner's Answer, page 5.) Appellants have demonstrated a utility for the claimed polynucleotides irrespective of whether or not a person would wish to perform additional experimentation on biological function of the polypeptide encoded by the claimed polynucleotide as another utility. The fact that additional experimentation could be performed to determine the functionality of the polypeptides encoded by the claimed polynucleotides does not preclude, and is in fact irrelevant to, the actual utility of the invention. That utility exists today regardless of the specific function of the polypeptides encoded by the claimed polynucleotides. The Examiner confuses use with function.

¹Appellants note that Claim 36 on appeal does not recite polypeptides but rather "[a]n isolated polynucleotide comprising. . .a naturally occurring polynucleotide sequence having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO:1. . ."

B. Use of claimed invention in toxicology testing

The Examiner alleges that the Coleman '100 application "is limited to teaching the use of 'said polynucleotides' which encode a human Jak2 kinase polypeptide as an enzymatic catalyst and provides no guidance with regard to other uses" and that "Appellants give none of the particulars of toxicology testing with the claimed polynucleotides having greater than 92% identity to SEQ ID NO:1."

(Examiner's Answer, pages 5 and 14.) However, well established uses, such as toxicology testing and gene expression monitoring, need not be explicitly described in the Specification. See the Bedilion Declaration e.g, at ¶¶ 10-12 for a discussion of the well-known use of naturally occurring polynucleotides in cDNA microarrays in toxicology testing and gene expression monitoring. Moreover, the Examiner's Answer fails to acknowledge, let alone address, the Coleman '100 disclosure on gene expression monitoring applications.

For example, the Coleman '100 application teaches that the chip technologies and the hjak2 nucleotide sequence:

can be used in a diagnostic test or assay to detect disorder or disease processes associated with abnormal expression of hjak2. The nucleotide sequence is added to a sample (fluid, cell or tissue) from a patient under hybridizing conditions. After an incubation period, the sample is washed with a compatible fluid which optionally contains a reporter molecule which will bind the specific nucleotide. After the compatible fluid is rinsed off, the reporter molecule is quantitated and compared with a standard for that fluid, cell or tissue. If hjak2 expression is significantly different from the standard, the assay indicates the presence of disorder or disease. The form of such qualitative or quantitative methods may include northern analysis, dot blot or other membrane-based technologies, dip stick, pin or chip technologies, PCR, ELISAs or other multiple sample format technologies. (Coleman '100 application at page 14, lines 24-36).

The Examiner states, on page 15 of the Examiner's Answer, that a skilled artisan could not use the claimed polynucleotides in gene expression monitoring (toxicology testing, drug development, and the diagnosis of disease) without undue experimentation. This argument amounts to nothing more than the Examiner's disagreement with the Bedilion Declaration (which purports therefore to substitute the Examiner's judgment for that of Appellants' expert) and Appellants' assertions about the knowledge of a person of ordinary skill. The Examiner must accept the Appellants' assertions to be true. The

Examiner is, moreover, wrong on the facts because Appellants demonstrate that the claimed invention can be used in gene expression monitoring to study questions completely independent from characterizing a “specific disease state” related to the claimed polynucleotides. For example, the claimed polynucleotides could be used to determine whether a drug is likely to have toxic effects. It is noted that the Examiner has failed to provide either evidence or sound scientific reasoning in support of his position.

C. Irrelevance of differential expression to utility in toxicology testing

The Examiner asserts that the specification does not disclose “any of the claimed *variant* polynucleotides (nor even SEQ ID NO:1) as markers for a specific disease state,” that “[a]bsent a disclosure of altered levels, structure, or function of a polynucleotide in a diseased cell or tissue as compared with the corresponding healthy cell or tissue, the polynucleotides of claim 36 parts b) and d) are not indicative of a disease state and do not provide an appropriate target for drug discovery or toxicology testing,” and that “[g]uidance relating the claimed polypeptide [*sic*: polynucleotide] variants to a specific disease state is necessary for the asserted uses of toxicology testing, drug discovery, and the diagnosis of disease.” (Examiner’s Answer, page 15, italics in original.)

Disease association or differential expression are irrelevant. Appellants need not demonstrate whether the claimed polynucleotides are associated with disease, or are differentially expressed. Appellants need only demonstrate that the claimed polynucleotides are useful.

The claimed polynucleotides can be used for toxicology testing in drug discovery without any knowledge of disease association or differential expression (see Appeal Brief and Response to Office Action filed June 13, 2001). Monitoring the expression of the polynucleotides gives important information on the potential toxicity of a drug candidate that is specifically targeted to any other polynucleotide or polypeptide, regardless of the disease association or differential expression of the claimed polynucleotides. The claimed polynucleotides are useful for measuring the toxicity of drug candidates specifically targeted to **other** polynucleotides or polypeptides, regardless of any possible utility for measuring the properties of the claimed polynucleotides.

This is a real-world use, available at the time of filing, and would not require “undue experimentation.” (Examiner’s Answer, page 15.)

D. Utility of all expressed polynucleotides in toxicology testing

The Examiner argues on page 14 of the Examiner's Answer that use of the claimed polynucleotides is not acceptable because it is "this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or polynucleotides, but is only potential with respect to the claimed polynucleotides. Further any potential diagnostic utility is not yet known and has not yet been disclosed." The Examiner does not point to any law, however, that says a utility that is shared by a large class is somehow not a utility. If all of the class of expressed human polynucleotides can be so used, then they all have utility. The issue is, once again, whether the polynucleotides have any utility, not whether other compounds have a similar utility. Nothing in the law says that an invention must have a "unique" utility. Indeed, the whole notion of "well-established" utilities PRESUPPOSES that many different inventions can have the exact same utility (if the Examiner's argument were correct, there could never be a well-established utility, because you could always find a generic group with the same utility!).

It is true that just about any expressed human polynucleotide will have use as a toxicology control, but Appellants need not argue this for the purposes of this case. Appellants argue only that this particular claimed invention could be so used, and has provided the Declaration of Bedilion back this up. The Examiner is completely wrong to characterize Appellants' argument regarding use as a control as somehow requiring the person using the invention to do further research to identify biological function. The point is not whether the claimed polynucleotides are, in any given toxicology test, differentially expressed. The point is that the invention provides a useful measuring stick regardless of whether there is or is not differential expression. That makes the invention useful today, in the real-world, for real purposes having nothing to do with further characterization of the invention itself.

E. Summary

The Examiner has provided neither evidence nor sound scientific reasoning to support the allegation that the use of the claimed polynucleotide variants is not enabled. The Examiner appears to base his allegation on personal opinion, as no evidence is provided to support his position dismissing the uses in toxicology testing and drug discovery discussed by Appellants in the Appeal Brief and in the Response filed June 13, 2001. The claimed polynucleotide variants are products of expressed genes.

Therefore, these naturally-occurring polynucleotide variants are useful for the same purposes as the polynucleotide of SEQ ID NO:1 in toxicology testing. These utilities are described fully in the Appeal Brief (Issue 1) and in the Response to Office Action filed June 13, 2001. (Appellants note that the Examiner did not address the uses of the claimed polynucleotide variants in toxicology testing in the Final Office Action, despite Appellants's arguments on this topic in the Response filed June 13, 2001.) This satisfies the "how to use" requirement of 35 U.S.C. § 112, first paragraph for the naturally-occurring variants of SEQ ID NO:1, as uses in gene expression monitoring analyses are adequate.

As set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Contrary to the standard set forth in *Marzocchi*, the Examiner has failed to provide any *reasons* why one would doubt that the guidance provided by the present Specification would enable one to use the naturally-occurring sequences at least 90% identical to SEQ ID NO:1. Hence, a *prima facie* case for non-enablement has not been established with respect to the recited variants of SEQ ID NO:1.

V. Written description rejection

Nowhere in the Reply Brief does the Examiner offer any evidence that one of ordinary skill in the art would not have understood, from the disclosure in the specification, along with "[w]hat is conventional or well known to one of ordinary skill in the art," that Appellants were in possession of "[a]n isolated polynucleotide comprising . . . a naturally occurring polynucleotide sequence having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO:1" In the Examiner's Answer, the Examiner ignores the claim limitation of "having greater than 92% sequence

identity to the polynucleotide sequence of SEQ ID NO:1” and attempts to introduce a “functional limitation” to the polynucleotide variants of the claims, limitations which are not present in Claims 36-40. The Examiner alleges that the “skilled artisan would not be able to envision all of the member [*sic*: members] of the claimed genus of polynucleotides merely from its structural limitations. This enormous genus will encompass a wide variety of polynucleotide with their own distinct properties. Because appellants have provided no functional limitation for the claimed polynucleotides, the single disclosed polynucleotide of SEQ ID NO:1 is not representative of the entire genus and one of skill in the art would not recognize that appellants were in possession of all polynucleotides comprising a naturally-occurring polynucleotide [sequence] having greater [than] 92% identity to SEQ ID NO:1.”

(Examiner’s Answer, page 18.)

The Examiner’s position is clearly contrary to the USPTO’s own written description guidelines (“Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1”, published January 5, 2001), which provide that:

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics⁴² which provide evidence that applicant was in possession of the claimed invention,⁴³ i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.⁴⁴ **What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.**⁴⁵ **If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.**⁴⁶ (emphasis added)

Here, there simply is no requirement that the claims recite particular variant polynucleotide sequences because the claims already provide sufficient structural definition of the claimed subject matter. That is, the polynucleotide variants are defined in terms of SEQ ID NO:1 (“polynucleotide comprising . . . a naturally occurring polynucleotide sequence having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO:1”). Because the claimed polynucleotide variants are defined in terms of SEQ ID NO:1, the precise chemical structure of every polynucleotide variant within the scope of the claims can be discerned. The Examiner’s position is nothing more than a misguided attempt to require Appellants to unduly limit the scope of their claimed invention.

The Examiner further alleges that “[w]hile one of skill in the art, provided the sequence of SEQ ID NO:1 with an nucleotide sequence sharing greater than 92% identity, one cannot recognize which of these variants occurs naturally and is thus encompassed by the genus of claim 36, part b).” (Examiner’s Answer, page 18.)

Appellants note that sequence information is not provided in a vacuum. Identification of the source of the sequence will typically allow one to determine if it is naturally-occurring. Also, attempted deceit to hide the source will not preclude infringement.

Further, functional limitations are not necessary as the structural and source limitations are sufficient to describe the claimed polynucleotide variants and in any case, “biological function” is irrelevant to the use of the claimed polynucleotide variants in toxicology testing.

The Examiner further states that “the claims of the ‘740 patent of the *Lilly* case were limited by *both* structural and functional limitations (see for example claim 4 of ‘740), thus placing the artisan in possession of the attributes and features of all members of the claimed genus.” (Examiner’s Answer, pages 21-22, italics in original.) Appellants note that Claim 4 of the ‘740 patent was not at issue in the *Lilly* case. As stated in the opinion (*University of California v. Eli Lilly and Co.*, 43 USPQ2d, 1401 (CAFC 1997), “[i]n 1990, UC brought this action in the Northern District of California, alleging that *Lilly* was infringing claims 1, 2, and 4-7 of the ‘525 patent under the doctrine of equivalents and infringing claims 2-3, 5-6, 8-10, and 13-14 of the ‘740 patent, either literally or under the doctrine of equivalents.”

VI. Written description rejection, new matter

The Examiner rejected Claims 36-40 under 35 U.S.C. §112, first paragraph, as allegedly containing new matter with respect to the recitation of “92% sequence identity” (see part b of claim 36).

As discussed above in connection with Issue Two, case law provides that to fulfill the written description requirement of 35 U.S.C. §112, first paragraph, “. . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the “written description” inquiry, *whatever is now claimed*”; *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Consideration

of the originally filed application shows that Appellants were in possession of what is now claimed, *i.e.*, “a naturally occurring polynucleotide sequence having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO:1.”

In this regard, see the following portions of the Specification:

“Naturally occurring HJAK2” refers to a polypeptide produced by cells which have not been genetically engineered or which have been genetically engineered to produce the same sequence as that naturally produced. (Specification at page 7, lines 8-10)

As a result of the degeneracy of the genetic code, a multitude of HJAK2-encoding nucleotide sequences may be produced and some of these will bear only minimal homology to the endogenous sequence of any known and naturally occurring Jak2 kinase sequence. This invention has specifically contemplated each and every possible variation of nucleotide sequence that could be made by selecting combinations based on possible codon choices. These combinations are made in accordance with the standard triplet genetic code as applied to the nucleotide sequence of naturally occurring HJAK2 and all such variations are to be considered as being specifically disclosed. (Specification at page 10, lines 4-12)

The assembled nucleotide sequence (SEQ ID No 1), *hjak2*, encodes the polypeptide (SEQ ID No 2), HJAK2. Computer search and alignment of the full length amino acid sequence showed that HJAK2 has 92% similarity to murine Jak2 kinase (MUSPTK1; GenBank GI 409584; Wilks AF (1989) Proc Nat Acad Sci 86:1603-7) which in turn has 96% sequence similarity with human Jak1 kinase. These homologies and the conserved residues, G₄₈, K₇₃, E₁₉₂, and D₂₂₀ which all lie within the catalytic domain contributed to the naming and uses of *hjak2*. (Specification at page 3, lines 29-36)

Before the present sequences, variants, formulations and methods for making and using the invention are described, it is to be understood that the invention is not to be limited only to the particular sequences, variants, formulations or methods described. The sequences, variants, formulations and methodologies may vary, and the terminology used herein is for the purpose of describing particular embodiments. The terminology and definitions are not intended to be limiting since the scope of protection will ultimately depend upon the claims. (Specification at page 9, lines 9-16)

Thus, while the originally filed application does not contain a verbatim recitation of the present “92% sequence identity” claim language, it is apparent that the inventors contemplated naturally occurring polynucleotide and polypeptide sequences of Jak2 kinase molecules. Moreover, the inventors were aware of the Wilks murine Jak2 kinase, which has 92% similarity to the amino acid

sequence of SEQ ID NO:2. Hence, it is axiomatic that the present inventors considered naturally occurring polynucleotide sequences having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO:1 as part of their invention, *i.e.*, those naturally occurring polynucleotide sequences which were not part of the prior art. See, for example, *In re Johnson et al.* (CCPA 1977) 588 F2d 1008, 194 USPQ 187 and *In re Wertheim et al.* (CCPA 1976) 541 F2d 257, 191 USPQ 90.

Accordingly, the “92% sequence identity” language appearing in part b of Claim 36 does not represent new matter.

VII. Obviousness rejection

The Examiner rejected Claims 37-40 under 35 U.S.C. §103(a) as being unpatentable over Silvennoinen et al. The Examiner alleged that “an oligomer of the polynucleotide comprising the nucleic acid sequence of SEQ ID NO:1 is made obvious by Silvennoinen” and that “[o]ne of ordinary skill in the art at the time of filing would be motivated to use the sequence taught by Silvennoinen et al. to design oligomers for use as primers to amplify and determine the level of mRNA encoding the murine Jak2 protein or to isolate other mRNAs encoding related proteins such as human Jak2 using hybridization or polymerase chain reaction methodology.” (Final Office Action, page 7.)

Appellants respectfully submit that the Examiner has mischaracterized Appellants’ claims, and continues to fail to give proper consideration to the entire claims in making the rejection.

Appellants’ rejected claims are as follows:

37. A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 36, the method comprising:

a) hybridizing the sample with a probe comprising at least 16 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

38. A method of claim 37, wherein the probe comprises at least 30 contiguous nucleotides.

39. A method of claim 37, wherein the probe comprises at least 60 contiguous nucleotides.

40. A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 36, the method comprising:

a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and

b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

Appellants note that in all four of claims, drawn to methods of detecting specific polynucleotides, the preamble to the claim contains the limitation "said target polynucleotide having a sequence of a polynucleotide of claim 36." In this case, the preamble "breathes life and meaning" into the claim and thus is a limitation which is **not** taught by the prior art. Moreover, it should be noted that the product of these methods is a complex or other product necessarily defined by the novel sequences of Claim 36.

Appellants respectfully submit that the rejection fails to state a proper *prima facie* case of obviousness, and that the rejection should, therefore, be reversed.

The Examiner has mischaracterized the claims

First and foremost, this rejection is inapt because the Examiner has failed to cite any references which, either alone or in combination, would render obvious the claimed methods, which relate to methods of detecting a specific, particular sequence. No matter how obvious it might have been to try to detect the specific full length sequence claimed in Claims 37-40, even assuming, *arguendo*, that it might be obvious to try to detect an unknown full length sequence based on the existence of a gene encoding a mouse Jak2 kinase in the prior art,

. . . [o]bvious to try" has long been held not to constitute obviousness. *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1680-81 (Fed. Cir. 1988). A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out. *In re Deuel*, 34 USPQ2d 1210 (CAFC 1995).

The Examiner alleges that the method of detecting a polynucleotide of SEQ ID NO:1 is obvious, because a mouse Jak2 kinase gene (e.g., the cited Silvennoinen et al. reference) was identified. However, it is respectfully pointed out that the mouse Jak2 kinase gene was NOT identified as being a part of Appellants' claimed sequence of SEQ ID NO:1, which had not yet been elucidated. What might have been obvious is the **wish to know** the human homolog of the mouse Jak2 kinase gene, but the Silvennoinen reference does not disclose the human sequence. Moreover, while it is also true that the Silvennoinen mouse Jak2 kinase gene sequence (or, more correctly, the complement thereof) **might** have been useful to detect the human Jak2 kinase full length sequence, it was not so used by Silvennoinen, and in any case, the corresponding human Jak2 kinase full length sequence of SEQ ID NO:1 was not known until Appellants elucidated it.

Appellants do not claim a method for detecting all polynucleotides encoding Jak2 kinases. Appellants claim a method for detecting **the** polynucleotides of Claim 36. The Examiner continues to improperly construe the claim language by failing to give weight to the limitation of the preamble "said target polynucleotide having a sequence of a polynucleotide of claim 36."

As was discussed in *Pitney Bowes Inc. v. Hewlett-Packard Co.*, 51 USPQ2d 1161 (Fed. Cir 1999):

If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is "necessary to give life, meaning, and vitality" to the claim, then the claim preamble should be construed as if in the balance of the claim. *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 480-81 (CCPA 1951); see also, 112 F.3d 473, 478, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997); *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1257, 9 USPQ2d 1962, 1966 (Fed. Cir. 1989). Indeed, when discussing the "claim" in such a circumstance, there is no meaningful distinction to be drawn between the claim preamble and the rest of the claim, for only together do they comprise the "claim".

Thus, it is clear that the Examiner cannot disregard the limitation recited in the preamble, i.e., that the product detected is a specific sequence, and that sequence is not only novel, it is unobvious itself. The only imaginable process of detection claim that might be obvious over the cited prior art would be the wish to find a naturally-occurring sequence that is fully complementary to the complement of the Silvennoinen mouse Jak2 kinase gene, i.e., a method of detecting the Silvennoinen mouse Jak2 kinase gene; that is **not** what Claims 37-40 encompass.

Therefore, Appellants submit that the Examiner has clearly failed to establish a proper *prima facie* case of obviousness, as

- 1) the Examiner has failed to construe the claims properly; and
- 2) the skilled worker could only, at best, have hoped to detect the exact complement of a complement to the Silvennoinen mouse Jak2 kinase gene, not the full length sequence of SEQ ID NO:1.

Thus, the cited art could not render the claimed methods obvious; since the entire sequence of SEQ ID NO:1 was not known, there was no way that detecting it, as compared to the Silvennoinen mouse Jak2 kinase gene, or any other related sequence, could be obvious.

The Examiner has further asserted that, using a polynucleotide of Silvennoinen et al., “it is common practice in the art to design oligomers such that they do not correspond exactly to the sequence on which they are based,” that “an oligomer of the polynucleotide comprising the nucleic acid sequence of SEQ ID NO:1 is made obvious by Silvennoinen et al.” and that “one of ordinary skill in the art would have been motivated to use these oligomers as part of a method for detecting the level of murine and human Jak2 mRNAs in tissue samples or identifying related mRNAs.” (Examiner’s Answer, page 10.)

To support an obviousness rejection under 35 U.S.C. § 103, “all the claim limitations must be taught or suggested by the prior art.” M.P.E.P. § 2143.03. The rejection focuses on the probes used in the claimed methods, and asserts that the Silvennoinen et al. document makes obvious the identity of particular probes which could be used to practice the recited methods of detection. Following this logic, the Examiner concludes that the methods are obvious because the probes are obvious. It may be possible that such logic would apply if the recited methods were directed to detecting any target polynucleotide which hybridizes to probes generated from the sequence of Silvennoinen et al. However, this is not the case with the recited methods of detection. The claims in question recite methods of detecting specific target polynucleotides which are disclosed in the specification. For example, claim 37 recites a method of “detecting a target polynucleotide in a sample, wherein said target polynucleotide having a sequence of a polynucleotide of claim 36.”

Claim 36 recites:

An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of:

- a) the polynucleotide sequence of SEQ ID NO:1,
- b) a naturally occurring polynucleotide sequence having greater than 92% sequence identity to the polynucleotide sequence of SEQ ID NO:1,
- c) a polynucleotide sequence complementary to a),
- d) a polynucleotide sequence complementary to b), and
- e) an RNA equivalent of a)-d).

The polynucleotides recited by claim 36 are free of prior art. The methods recited by claim 37-40 are directed toward detecting a target polynucleotide **having the sequence of the polynucleotides recited by claim 36.**

The rejection is not supported because it ignores the limitation that the claims are directed to detecting specific **target polynucleotides**, disclosed in the specification. One cannot practice the recited methods of detecting a target polynucleotide if one does not know the identity of that target polynucleotide, or even whether that target polynucleotide exists. Without knowledge of a target polynucleotide, one would not have any conception of practicing a method of detecting it, one would not have any motivation to attempt to detect it, and one would certainly not have the ability to detect it. By focusing on the alleged obviousness of the probes used in the claimed methods, the Examiner has ignored the fact that the claimed methods require detection of the recited **target polynucleotides**. Since there is no suggestion or teaching in the art to detect the recited target polynucleotides, one would not have been guided to practice the claimed methods.

Appellants note that the dictionary defines “specific” as “restricted to a particular individual, situation, relation, or effect.” (Reference No. 1; Merriam-Webster’s Collegiate Dictionary; Merriam-Webster OnLine: <http://www.m-w.com>.) Hence, the phrase “specifically hybridizes” indicates that the probes of Claims 37-39 bind only to the polynucleotides of Claim 36 and thus would not by definition bind to any oligomer, if any, taught by Silvennoinen et al. It is well known and an inherent requirement of the method that the primers used in PCR amplification must specifically hybridize to the target polynucleotide.

Furthermore, Silvennoinen et al. do not teach a degenerate probe suitable for using to detect the polynucleotides of Claim 36. Though one of skill in the art may well attempt to design degenerate

probes from especially those which would specifically hybridize to the polynucleotides of Claim 36, could not be foreseen from the Silvennoinen et al. document.

Silvennoinen et al. do not teach or suggest the detection of the target polynucleotides recited in the claims. Since this reference does not teach or suggest all of the claim limitations, the requirements for a *prima facie* showing of obviousness under 35 U.S.C. § 103 have not been met.

For at least the above reasons, this rejection should be overturned.

VIII. Double Patenting Rejection of Claims 30-36

Claims 30-36 were rejected under the judicially created doctrine of double patenting over Claims 1-3 of U.S. Patent No. 5,914,393, with the Examiner relying on the case of *In re Schneller*, 158 USPQ 210 (CCPA 1968). While not conceding the propriety of the Examiner's position, Appellants are willing to submit a Terminal Disclaimer with respect to U.S. Patent No. 5,914,393 in the interest of expediting prosecution of the subject application, upon indication that the application is otherwise allowable. Therefore, it is requested that the Board indicate that the subject application will be allowable upon submission of such a Terminal Disclaimer.

IX. Double Patenting Rejection of Claims 37-40

Claims 37-40 were rejected under the judicially created doctrine of obviousness-type double patenting over Claims 1-3 of U.S. Patent No. 5,914,393. While not conceding the propriety of the Examiner's position, Appellants are willing to submit a Terminal Disclaimer with respect to U.S. Patent No. 5, 914, 393 in the interest of expediting prosecution of the subject application, upon indication that the application is otherwise allowable. Therefore, it is requested that the Board indicate that the subject application will be allowable upon submission of such a Terminal Disclaimer.

X. Conclusion

For all the foregoing reasons and the reasons stated in Appellants' Brief on Appeal, it is submitted that the Examiner's rejections of the claims on appeal should be reversed.

If the USPTO determines that any additional fees are due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108**.

This brief is enclosed in triplicate.

Respectfully submitted,
INCYTE GENOMICS, INC.

Date: September 30, 2002

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8 entries found for **specific**.
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specific gravity
specific heat

Main Entry: **specific**

Pronunciation: spi-'si-fik

Function: *adjective*

Etymology: Late Latin *specificus*, from Latin *species*

Date: circa 1631

1 **a** : constituting or falling into a specifiable category **b** : sharing or being those properties of something that allow it to be referred to a particular category

2 **a** : restricted to a particular individual, situation, relation, or effect <a disease *specific* to horses> **b** : exerting a distinctive influence (as on a body part or a disease) <*specific* antibodies>

3 : free from ambiguity : ACCURATE <a *specific* statement of faith>

4 : of, relating to, or constituting a species and especially a biologic species

5 **a** : being any of various arbitrary physical constants and especially one relating a quantitative attribute to unit mass, volume, or area **b** : imposed at a fixed rate per unit (as of weight or count) <*specific* import duties> -- compare AD VALOREM

synonym see SPECIAL, EXPLICIT

- spec-i-fi-cally /-fi-k (&-)l/ *adverb*

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Pronunciation Symbols

\ə as a and u in abut	\e as e in bet	\ə as aw in law
\i as e in kitten	\e as ea in easy	\ɔɪ as oy in boy
\ər as ur/er in further	\g as g in go	\θ as th in thin
\ə as a in ash	\l as l in hit	\θ as th in the
\ə as a in ace	\l as l in ice	\l as oo in loot
\ə as o in mop	\j as j in job	\l as oo in foot
\əʊ as ou in out	\ŋg as ng in sing	\j as y in yet
\tʃ as ch in chin	\o as o in go	\zʃ as sl in vision

For more information see the Guide To Pronunciation.



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